Pituitary-dependent and adrenal tumor hyperadrenocorticism: which treatment is best?

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The method of treatment must be carefully chosen based on the cause (PDH or AT) of disease, age and condition of the patient and presence of concomitant disease. Cost and availability of treatment methods as well as frequency of follow-up evaluations are also important considerations. Before treatment options can be discussed with the owner the form of hyperadrenocorticism (HAC) should be known. Adrenal ultrasonography and measurement of endogenous ACTH are the diagnostic tools which enable discrimination between PDH and AT in the majority of dogs. In dogs in which PDH is confirmed we highly recommend evaluation of the size of the pituitary mass by means of CT or MRI, in particular in dogs in which the low-dose dexamethasone test showed so-called dexamethasone resistance. 10 – 15% of dogs with PDH have a large pituitary mass; those dogs are in danger to develop neurological signs additionally to the signs of cortisol excess. If the mass is in fact large (approximately > 8 mm in height) in a particular patient we recommend to perform radiation therapy. However, the owner needs to understand that radiation therapy aims to reduce tumor size and improvement or prevention of neurological signs, it usually does not lead to a disappearance of the endocrine signs, such as polyuria/polydipsia, polyphagia, hair loss, panting. Most masses shrink in size considerably within days to weeks. Three to four weeks after the end of radiation therapy the patient is re-evaluated in particular with regard to clinical signs of cortisol excess, e.g. pu/pd, polyphagia, panting. If they are still present (which is usually the case) we start with medical treatment. In dogs with a small pituitary mass we discuss that there are two treatment options: medical treatment and surgery. During the last decade transsphenoidal pituitary surgery has been established as a valuable treatment option for dogs with PDH. Most dogs with PDH can be "cured" by this approach however, lifelong supplementation with thyroxine and glucocorticoids is usually needed. Pituitary surgery is possible only in a few specialized veterinary institutions and requires a team approach, involving a neurosurgeon, an endocrinologist and a radiologist. Transsphenoidal hypophysectomy has the potential to become the treatment of choice for dogs (and cats) with PDH and owners are often extremely satisfied with the outcome.
Vetoryl (trilostane) is the only drug licensed for the treatment of canine HAC. The drug has been evaluated in many clinical studies and has been found to be efficacious and usually well tolerated. In 80 – 85% of dogs with HAC clinical signs such as pu/pd, panting and lethargy disappear or improve substantially within a few weeks. Hair coat abnormalities may need several months for improvement, some dogs may have transient worsening of their dermatologic problems before clinical improvement. Polyphagia often persists or decreases only marginally. Treatment protocols vary between institutions. In Zurich we currently start therapy with 2 mg/kg Vetoryl SID, administered in the morning with food. Re-evaluations are scheduled after 2, 4, 8, 12 – 16 weeks and then every 6 months. The ACTH stimulation test is used to monitor treatment and is performed 2 – 3 hours after the application of the drug. A post ACTH cortisol concentration between 2 – 5 µg/dl (55 – 135 mmol/l) is considered an appropriate response. If clinical improvement is unsatisfactory after approximately 12 weeks we discuss BID instead of SID application with the owner. Since we do not use more than 60 mg/dog/day as initial dosage we have not seen any serious side effects such as adrenal necrosis.

Surgical removal is the treatment of choice for adrenal tumors, providing that there is no wide-spread tumor invasion and the dog is not debilitated. Adrenalectomy is technically challenging and should be performed by a skilled surgeon. Approximately 30 - 50 per cent of patients develop severe postoperative complications, which include hemorrhage pancreatitis, pneumonia, pulmonary thromboembolism, acute renal failure, sepsis and hypoadrenocorticism due to insufficient steroid levels. It is not known whether dogs with AT that undergo long-term medical treatment before adrenalectomy, have fewer postoperative complications and higher survival rates. Autonomous cortisol secretion results in atrophy of the cells of the zona fasciculata and zona reticularis, and in a few dogs the aldosterone-producing cells of the zona glomerulosa. Thus glucocorticoid substitution intraoperatively and postoperatively is necessary. Mineralocorticoid treatment is instituted when required. Intravenous fluids (0.9% NaCl or Ringer`s solution) should be administered at a maintenance rate at the start of anaesthesia, during surgery and the postoperative period. When the tumor is located, dexamethasone should be given at a dosage of 0.1 mg/kg over a 6-hour period. The dose should be repeated until oral medication can be started. An alternative to dexamethasone is hydrocortisone, which can be given at a dosage of 4 to 5 mg/kg, intravenously, during surgery, and then at 1 mg/kg, intravenously, every 6 hours until oral medication is started. Prednisolone is then administered orally approximately as follows: 1 mg/kg BID for 2 to 3 days, 0.5 mg/kg BID for 2 to 3 days, 0.25 mg/kg BID for 3 weeks, 0.25 mg/kg SID for 3 weeks, 0.25 mg/kg every other day for 3 weeks, and then 0.25 mg/kg every 3 days. Prednisolone can usually be discontinued after 2 to 3 months. The ACTH stimulation test is helpful for evaluation of adrenal function.

References

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